



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
-----------------	-------------	----------------------	---------------------	------------------

10/719,913

11/21/2003

Gary A. Dahl

EPICEN-09580

3340

72960

7590

09/03/2008

Casimir Jones, S.C.
440 Science Drive
Suite 203
Madison, WI 53711

EXAMINER

STAPLES, MARK

ART UNIT

PAPER NUMBER

1637

MAIL DATE

DELIVERY MODE

09/03/2008

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/719,913	Applicant(s) DAHL ET AL.	
	Examiner Mark Staples	Art Unit 1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 06/09/2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 7-40 is/are pending in the application.
- 4a) Of the above claim(s) 8, 9, 11-15, 31-35, and 39 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 7, 10, 16-30, 36-38 and 40 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--------------------------------------------------------------------------------------|-------------------------------------------------------------------|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 06/09/2008 has been entered.

2. Applicant's amendment of claims 7, 26, 60, and 36 in the paper filed on 06/09/2008 is acknowledged.

Claims 7,10,16-30, 36-38, and 40 are pending and at issue.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Rejections that are Withdrawn

Claim Rejections Withdrawn - 35 USC § 102(b)

3. The rejection of claims 7, 10, 16-24, 26, 28, 30, 36, 38, and 40 under 35 U.S.C. 102(b) as being anticipated by Lorincz et al. (Feb. 2000) is withdrawn. Applicant's arguments have been considered but are moot in view of the new ground(s) of rejection, necessitated by amendments to the claims.

Claim Rejections Withdrawn - 35 USC § 103(a)

4. The rejection of claims 25, 27, 29, and 37 under 35 U.S.C. 103(a) as being unpatentable over Lorincz et al. further in view of Hall et al. (1999) is withdrawn. Applicant's arguments have been considered but are moot in view of the new ground(s) of rejection, necessitated by amendments to the claims.

Rejections Necessitated by Amendment

Claim Rejections - 35 USC § 103

5. Claims 7, 10, 16-24, 26, 28, 30, 36, 38, and 40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Soares et al. (United States Patent 5,830,662 issued November 3, 1998) and Lorincz et al. (US Patent No. 6,136,535, issued Feb. 2000, previously cited).

Regarding claim 7, Soares et al. teach methods for making transcription products corresponding to a target nucleic acid sequence in a target nucleic acid in a sample (entire patent, especially the claims, claims 1-25), the method comprising the steps of: (1) primer extending a sense promoter primer (see column 14 lines 22-37 for the promoter within the RNA and claims 7 and 8 for the RNA precursor) to generate a first-strand cDNA using a target nucleic acid which is also cDNA as a template (comprising the additional preliminary step as taught by Soares et al. of first transcribing the RNA into target cDNA, again see claims 7 and 8), the sense promoter primer comprising a 5'-end portion comprising a sense transcription promoter and a 3'-end portion that is

Art Unit: 1637

complementary to the 3'-end of the target cDNA sequence since the promoter within the RNA is inherently complementary to the target cDNA sequence;

(2) ligating the 5' and 3' ends of the resulting sense promoter-containing first-strand cDNA to each other to obtain a single-stranded circular sense promoter-containing first-strand cDNA by teaching a ligation reaction that promotes recircularization, that is of the what is recited in the instant claims as the first-strand cDNA (see column 12 lines 4 and 5);

(3) annealing an appropriate oligonucleotide/primer to the first-strand cDNA to obtain a transcription substrate (see claim 1 step 1 b); and

(4) transcribing the transcription substrate to make transcription products corresponding to the target nucleic acid sequence (see claim 1 steps 1 b to 1 e).

Regarding claim 1, while Sores et al. teach annealing an appropriate primer/oligonucleotide to the first strand to transcribe that strand, Soares et al. do not specifically teach the limitation of:

(3) annealing an anti-sense promoter oligonucleotide to the sense promoter containing first-strand cDNA to obtain a transcription substrate.

Regarding claim 10, Sores et al. teach using using the transcription products as the target nucleic acids (see claims 5, 19, and 23).

Regarding claims 7, 10, 16-22, 24, 28, 30, 36, 38, and 40, Lorincz et al. (Feb. 2000) teach a method comprising the steps of:

Art Unit: 1637

(1) obtaining said target nucleic acid (see Figure 1A and see claim 1 or 7 where the target nucleic acids may be a sample; see column 17 lines 14-16: "This process is capable of analyzing multiple samples sequentially or simultaneously"; and see column 3 lines 15 and 16: "Any nucleic acid may be amplified by the method of the present invention");

(2) obtaining said sense promoter primer, the sense promoter primer comprising a 5'-end portion comprising a sense transcription promoter and a 3'-end portion that is complementary to the target (see Figure 1A and see claim 1 or 7);

(3) annealing [hybridizing] the sense promoter primer with the target nucleic acid so as to form a target nucleic acid-sense promoter primer complex (see Figure 1A and see claim 1 or 7);

(4) contacting the target nucleic acid-sense promoter primer complex with a polymerase under polymerization reaction conditions to obtain first-strand nucleic acid that is complementary to the target sequence (see Figure 1A and see claims 1 and 6, or 7 and 11);

(5) ligating the first-strand nucleic acid to itself under ligation conditions so as to obtain circular sense promoter-containing first-strand nucleic acid (see column 4 lines 3 and 4: "Optionally, a ligation reaction may be carried out to fill the gap between the promoter and the template");

(6) obtaining an anti-sense promoter oligonucleotide (see Figure 4 and the circle T7 oligo given there and note that this anti sense promoter is attached to and antibody which an analyte binding substance, ABS);

Art Unit: 1637

(7) annealing the anti-sense promoter oligonucleotide to the circular sense promoter-containing first-strand nucleic to obtain a circular transcription substrate (see Figure 4); and

(8) contacting the circular transcription substrate with an RNA polymerase under transcription conditions wherein a transcription product is obtained (see Figure 4 for amplification of the circular substrate with polymerase to obtain additional product. And for use of an RNA polymerase see column 3 lines 54-57: "This product is subjected to transcription using, for example, RNA polymerase. In this way, a template DNA [transcription substrate] can be indirectly amplified without the need to carry out any cycled reaction").

Regarding claims 16 and 17, Lorincz et al. (Feb. 2000) teach a method using a wild type T7 RNA polymerase (see column 11, lines 23-25).

Regarding claim 18, Lorincz et al. (Feb. 2000) teach a method using four dNTPs (dATP, dGTP, dCTP, dTTP) four NTPs (ATP, GTP, CTP, UTP), see column 23, lines 17-20.

Regarding claim 19, Lorincz et al. (Feb. 2000) teach an *in vitro* method (see column 2 lines 61-64).

Regarding claim 22, Lorincz et al. (Feb. 2000) teach a method using messenger RNA, mRNA (see column 5 lines 7).

Regarding claims 23 and 40, Lorincz et al. (Feb. 2000) teach a synthetic promoter (see Example 1 for synthetic promoter-primer).

Regarding claim 24, Lorincz et al. (Feb. 2000) teach a target specific sequence (see claim 1).

Regarding claim 26 and 30, Lorincz et al. (Feb. 2000) teach a method for amplifying the amount of a template-complementary product, the method comprising the steps of:

(1) obtaining a transcription product (see Figure 1A and see claim 1 or 7; see column 3 lines 15 and 16: "Any nucleic acid may be amplified by the method of the present invention"; and see column 6 lines 23 and 24: "generating multiple RNA transcripts", nucleic acids, which are transcription products);

(2) obtaining a sense promoter primer comprising a 3'-end portion that is complementary to the 3'-end of the transcription product (see Figure 1A and see claim 1 or 7;);

(3) annealing [hybridizing] the sense promoter primer to the transcription product (see Figure 1A and see claim 1 or 7);

(4) primer-extending the sense promoter primer annealed to the transcription product acid with a DNA polymerase under DNA synthesis conditions to obtain first-strand cDNA (see Figure 1A and see claims 1 and 6, or 7 and 11; see column 3 lines 15 and 16: "Any nucleic acid may be amplified by the method of the present invention"; and see column 13 line 30-32: "Transcripts may also be subjected to a reverse transcriptase reaction in order to generate cDNAs . . . ");

Art Unit: 1637

(5) ligating the first-strand cDNA, wherein the 5'-end is covalently joined to the 3'-end of the first-strand cDNA to obtain circular sense promoter-containing first-strand DNA (see column 4 lines 3 and 4: "Optionally, a ligation reaction may be carried out to fill the gap between the promoter and the template");

(6) annealing an anti-sense promoter oligonucleotide to the circular sense promoter-containing first-strand cDNA to obtain a circular substrate for transcription (see Figure 4 for circle T7 oligo); and

(7) contacting the circular substrate for amplification with a RNA polymerase under conditions to obtain additional transcription product (see Figure 4 for amplification of the circular substrate with polymerase to obtain additional product).

Regarding claims 28 and 38, Lorincz et al. (Feb. 2000) teach a wash step that removes the RNA hybrid (annealed RNA) from other components (see Example 2, especially line 38).

Regarding claims 36, Lorincz et al. (Feb. 2000) teach a method for amplifying an amount of template-complementary transcription product, the method comprising:

(1) obtaining a transcription product by transcription of a template of a probe that is complexed with an analyte binding substance-oligo (see Figure 4 and claims 7, 10, 13, and 16; see column 3 lines 15 and 16: "Any nucleic acid may be amplified by the

Art Unit: 1637

method of the present invention”; and see column 6 lines 23 and 24: “generating multiple RNA transcripts”, nucleic acids, which are transcription products);

(2) obtaining a sense promoter primer comprising a 3'-end portion that is complementary to the 3'-end of the transcription product (see Figure 4 and claims 7 10, 13, and 16);

(3) annealing the sense promoter primer to the transcription product;

(4) primer-extending the promoter primer annealed to the transcription product with an RNA-dependent DNA polymerase under DNA synthesis conditions so as to obtain first-strand cDNA (see column 13 lines 9-11: “Transcripts may also be subjected to a reverse transcriptase reaction in order to generate cDNAs which may be analyzed”);

(5) ligating the first-strand cDNA, wherein the 5'-end is covalently joined to the 3'-end of the first-strand cDNA so as to obtain circular sense promoter-containing first-strand cDNA (see column 4 lines 3 and 4: “Optionally, a ligation reaction may be carried out to fill the gap between the promoter and the template”);

(6) annealing an anti-sense promoter oligo to the circular sense promoter-containing first-strand cDNA so as to obtain a circular substrate for transcription (see Figure 4 and the circle T7 oligo given there);

(7) contacting the circular substrate for transcription with an RNA polymerase under transcription conditions so as to obtain additional transcription product; and

(8) obtaining the additional transcription product (for claims 7 and 8 see Figure 4 for amplification of the circular substrate with polymerase to obtain additional product. And

Art Unit: 1637

for use of an RNA polymerase see column 3 lines 54-57: "This product is subjected to transcription using, for example, RNA polymerase. In this way, a template DNA [transcription substrate] can be indirectly amplified without the need to carry out any cycled reaction").

Regarding claims 7, 26, 30, and 36, Lorincz et al. (Feb. 2000) teach circular cDNA which is partially single-stranded (that is circular cDNA which is a duplex of single and double strands), but do not specifically teach circular cDNA which is completely single-stranded.

Therefore, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the methods of Lorincz et al. by using the circular cDNA which is completely single-stranded as suggested by Soares et al. with a reasonable expectation of success. The motivation to do so is provided by Soares et al. who teach that normalized cDNA libraries can be generated by propagation in single-stranded circle form (see Abstract). Thus, the claimed invention as a whole was *prima facie* obvious over the combined teachings of the prior art.

6. Claims 25, 27, 29, and 37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Soares et al. and Lorincz et al. as applied to claims 26 and 36 above, and further in view of Hall et al. (US Patent No. 5,994,069, issued 1999, previously cited).

Art Unit: 1637

Soares et al. and Lorincz et al. teach as noted above and teach a 3' end labeled phosphate labeled promoter primer, which is a synthetic primer promoter.

Soares et al. and Lorincz et al. do not specifically teach a promoter primer comprising a phosphate group on its 5' end.

Hall et al. (1999) teach labeling the 5' end (see claims 9 and 12).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the method of Soares et al. and Lorincz et al. by labeling, instead of the 3' end, the 5' end of a oligonucleotide promoter primer with a phosphate group as suggested by Hall et al. with a reasonable expectation of success. The motivation to do so is provided by Hall et al. who teach the successful detection of oligonucleotides which are labeled on the 5' end. Thus, the claimed invention as a whole was *prima facie* obvious over the combined teachings of the prior art.

Conclusion

7. No claim is free of the prior art.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark Staples whose telephone number is (571) 272-9053. The examiner can normally be reached on Monday through Thursday, 9:00 a.m. to 6:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Art Unit: 1637

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Mark Staples
/M. S./
August 21, 2008

/Kenneth R Horlick/
Primary Examiner, Art Unit 1637